

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claims 1-21 (cancelled)

Claim 22 (withdrawn-currently amended): A composition comprising a plurality of a conjugate, wherein said conjugate is formable by the conjugation of:

(a) ~~an ethyleneoxide~~ a -OCH₂CH₂O- containing chemically defined valency platform molecule comprising a moiety selected from -CH₂(CH₂OCH₂)_rCH₂-, 2,2'-ethylenedioxydiethylamine, triethylene glycol, and polyethylene glycol having a molecular weight of about 200 to about 8,000, wherein:

$r = 0$ to 300;

the moiety is derivatized with branching groups;

the valency of said platform molecule is provided by four or more attachment sites located at termini of the valency platform molecule;

the valency platform molecule has a single line of symmetry; and

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites for biologically active molecules; and

(b) a multiplicity of biologically active molecules conjugated to the chemically defined valency platform molecule at said attachment sites.

Claim 23 (withdrawn): The composition of claim 22, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 24 (cancelled)

Claim 25 (cancelled)

Claim 26 (withdrawn): The composition of claim 22, wherein the biologically active molecules comprise a polynucleotide.

Claim 27-31 (cancelled)

Claim 32 (withdrawn-currently amended): The composition of claim 22 [[or 64]], wherein the biologically active molecules are molecule is selected from the group consisting of carbohydrates, lipids, lipopolysaccharides, peptides, proteins, glycoproteins, and drugs.

Claim 33-34 (cancelled)

Claim 35 (withdrawn): The composition of claim 22, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 36 (withdrawn-currently amended): The composition of claim 35 [[or 77]], wherein the composition is suitable for the suppression of antibody production.

Claim 37 (cancelled)

Claim 38 (withdrawn-currently amended): The composition of claim 35 [[or 77]], wherein the composition is suitable for the treatment of human systemic lupus erythematosus.

Claim 39-42 (cancelled)

Claim 43 (withdrawn): The composition of claim 22, wherein the valency platform molecule comprises triethylene glycol.

Claim 44 (cancelled)

Claim 45 (withdrawn-currently amended): A method of making the composition of claim 22 [[or 64]], wherein the biologically active molecules are molecule is a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is at least [[about]] 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 46 (withdrawn): The composition of claim 22, wherein the conjugate comprises triethyleneglycol.

Claim 47-50 (cancelled)

Claim 51 (withdrawn-currently amended): The composition of claim 35 [[or 77]], wherein the composition is suitable for reducing antibody levels.

Claim 52 (withdrawn-currently amended): The composition of claim 35 [[or 77]] wherein at least one molecule of the biologically active molecules is an analog of an immunogen that binds specifically to an antibody to which the immunogen binds specifically and lacks T cell epitopes.

Claim 53 (withdrawn): The composition of claim 22 or 64, wherein the composition is suitable for reducing antibody levels.

Claim 54 (withdrawn): The composition of claim 22, wherein the conjugate comprises linking moieties bound to the valency platform molecule and to the biologically active molecules.

Claim 55-63 (cancelled)

Claim 64 (withdrawn-currently amended): A composition comprising a plurality of a conjugate, wherein said conjugate is formable by the conjugation of:

(a) an ethyleneoxide a -OCH₂CH₂O- containing chemically defined valency platform molecule comprising a moiety selected from -CH₂(CH₂OCH₂)_rCH₂-, 2,2'-ethylenedioxydiethylamine, triethylene glycol, and polyethylene glycol having a molecular weight of about 200 to about 8,000, wherein:

r = 0 to 300;

the moiety is derivatized with branching groups;

the valency of said platform molecule is provided by four or more attachment sites located at termini of the valency platform molecule; and

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites for biologically active molecules; and

(b) a multiplicity of biologically active molecules conjugated to the chemically defined valency platform molecule at said attachment sites.

Claim 65 (withdrawn): The composition of claim 64, wherein the valency platform molecule has a single line of symmetry.

Claim 66 (withdrawn): The composition of claim 64, wherein the biologically active molecules are the same.

Claim 67 (withdrawn): The composition of claim 64 or 66, wherein said conjugate comprises two branching groups, providing a total of four attachment sites for the biologically active molecules.

Claim 68 (withdrawn-currently amended): The composition of claim 64 [[or 66]], wherein the biologically active molecules comprise a polynucleotide.

Claim 69 (withdrawn): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex.

Claim 70 (withdrawn): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex of about 20 to about 50 base pairs in length.

Claim 71 (withdrawn): The composition of claim 68, wherein the polynucleotide is synthetic.

Claim 72 (withdrawn): The composition of claim 68, wherein the polynucleotide is prepared by molecular cloning.

Claim 73 (withdrawn): The composition of claim 68, wherein the polynucleotide is a polynucleotide duplex having a B DNA type helical structure.

Claim 74 (withdrawn): The composition of claim 64, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 75 (withdrawn): The composition of claim 64, wherein the biologically active molecules are selected from the group consisting of analogs of immunogens, haptens, mimotopes, and aptamers.

Claim 76 (withdrawn): The composition of claim 64, wherein the chemically defined valency platform molecule is substantially nonimmunogenic.

Claim 77 (withdrawn): The composition of claim 64 or 74, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 78 (cancelled)

Claim 79 (withdrawn): The composition of claim 77, wherein the composition is suitable for injection.

Claim 80 (withdrawn-currently amended): The composition of claims 22, 64 or 74 ~~claim 64 or 74~~, wherein the valency platform molecule comprises polyethylene glycol having a molecular weight of about 200 to about 8,000.

Claim 81 (withdrawn-currently amended): The composition of claims 22, 64 or 74, wherein the conjugate comprises a moiety having the formula -CH₂(CH₂OCH₂)_rCH₂- , wherein r = 1 to 300.

Claim 82 (withdrawn-currently amended): The composition of claims 22, 64 or 74, wherein the valency platform molecule comprises a moiety having the formula -CH₂(CH₂OCH₂)_rCH₂- , wherein r = 1 to 300.

Claim 83 (cancelled)

Claim 84 (withdrawn): The composition of claim 64 or 74, wherein the valency platform molecule comprises triethylene glycol.

Claim 85 (cancelled)

Claim 86 (withdrawn): The composition of claim 64, wherein the valency platform molecules have substantially homogeneous molecular weight.

Claim 87 (cancelled)

Claim 88 (cancelled)

Claim 89 (withdrawn): The composition of claim 64 or 74, wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.

Claims 90-98 (cancelled)

Claim 99 (withdrawn-currently amended): The conjugate according to claim 89, wherein the linking group is derived selected from the group consisting of a thio-6 carbon chain phosphate or [[and]] a thio-6 carbon chain phosphorothioate.

Claim 100 (withdrawn-currently amended): The conjugate of claim 89, wherein the linking group is derived from ~~comprises~~ an alkylsulphydryl moiety and the attachment sites comprise thiophilic groups.

Claim 101 (withdrawn): The conjugate of claim 64 or 74, wherein the attachment sites are thiophilic groups.

Claim 102 (withdrawn): The conjugate of claim 101, wherein the thiophilic groups are selected from the group consisting of haloacetyl, alkyl halide, alkyl sulfonate, maleimide, α,β -unsaturated carbonyl, alkyl mercurial, sulphydryl, and α,β -unsaturated sulfone.

Claim 103 (withdrawn): The conjugate of claim 101 wherein the attachment sites are selected from a maleimide, α -haloacetyl group or other appropriate Michael acceptor.

Claim 104 (withdrawn): The conjugate of claim 103, wherein the attachment sites are α -haloacetyl groups.

Claim 105 (withdrawn): The conjugate of claim 104, wherein the α -haloacetyl is bromoacetyl.

Claim 106 (currently amended): A conjugate formable by the conjugation of:

(a) ~~an ethyleneoxide a~~ $-OCH_2CH_2O-$ containing chemically defined valency platform molecule, wherein:

the valency platform molecule comprises branching groups that are derived from a diamino acid, triamine or amino diacid;

the valency of said platform molecule is provided by four or more attachment sites located at termini of the valency platform molecule; and

the valency platform molecule is chemically defined in that the number of branching groups pre-determines the number of attachment sites; and

(b) a multiplicity of polynucleotides.

Claim 107 (previously presented): The conjugate of claim 106, wherein the polynucleotides comprise a polynucleotide duplex.

Claim 108 (currently amended): The conjugate of claim 106 or 107, wherein each of the polynucleotides comprises at least [[about]] 20 nucleotides.

Claim 109 (previously presented): The conjugate of claim 106, wherein each of said polynucleotides comprises a single stranded polynucleotide consisting of approximately 20 alternating cytosine (C) and adenosine (A) nucleotides.

Claim 110 (previously presented): The conjugate of claim 109, wherein a second single stranded polynucleotide consisting of approximately 20 alternating thymidine (T) and guanosine (G) nucleotides is annealed to each of said single stranded polynucleotides that consists of approximately 20 alternating cytosine (C) and adenosine (A) nucleotides to form a double-stranded polynucleotide conjugate.

Claim 111 (currently amended): The conjugate of claim 26, 64, or 107, wherein said polynucleotides individually comprise the polynucleotide duplex of the formula:



Claim 112 (cancelled)

Claim 113 (previously presented): The conjugate of claim 106 or 110, wherein said polynucleotides are individually bound to the valency platform molecule via the 5' end of the polynucleotides.

Claim 114 (previously presented): The conjugate of claim 106, 110 or 111, wherein the polynucleotides are individually bound to the valency platform molecule via linker molecules.

Claim 115 (currently amended): The conjugate of claim 114 wherein each of the linker molecules is ~~selected from~~ derived from a thio-6 carbon chain phosphate or a thio-6 carbon chain phosphorothioate.

Claim 116 (currently amended): The conjugate of claim 114, wherein the linker molecules are derived from ~~are each~~ an alkylamino or alkylsulphydryl moiety.

Claim 117 (currently amended): The conjugate of claim 116, wherein the linker molecules are derived from ~~are each~~ an alkylsulphydryl moiety.

Claim 118 (currently amended): The conjugate of claim 116, wherein the alkylamino or alkylsulphydryl moiety is bound to ~~introduced to~~ the polynucleotide by phosphoramidite chemistry.

Claim 119 (previously presented): The conjugate of claim 106, 110 or 111, wherein the attachment sites are thiophilic groups.

Claim 120 (previously presented): The conjugate of claim 119, wherein the thiophilic groups are selected from the group consisting of haloacetyl, alkyl halide, alkyl sulfonate, maleimide, α,β -unsaturated carbonyl, alkyl mercurial, sulphydryl, and α,β -unsaturated sulfone.

Claim 121 (previously presented): The conjugate of claim 119 wherein the attachment sites are selected from a maleimide, α -haloacetyl group or other appropriate Michael acceptor.

Claim 122 (previously presented): The conjugate of claim 119, wherein the attachment sites are α -haloacetyl groups.

Claim 123 (previously presented): The conjugate of claim 119, wherein the α -haloacetyl is bromoacetyl.

Claim 124 (previously presented): A composition comprising the conjugate of claim 106; 110 or 111 in a pharmaceutically acceptable carrier.

Claim 125 (previously presented): The conjugate of claim 106, 110 or 111, formulated with a pharmaceutically acceptable injectable vehicle.

Claim 126 (cancelled):

Claim 127 (previously presented): The composition of claim 112, wherein the composition is suitable for the treatment of human systemic lupus erythematosis.

Claim 128 (currently amended): A method of making the conjugate of claim 107, the method comprising:

reacting (a) a multiplicity of single-stranded polynucleotides, each of which is at least [[about]] 20 nucleotides in length and has a functional group at or proximate one of its termini which is optionally derivatized with a linker group, with (b) attachment sites on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotide conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 129 (withdrawn): A method of making the composition of claim 64 or 106, the method comprising forming said conjugates by covalently bonding the biologically active molecules to the chemically-defined valency platform molecule to form a conjugate.

Claim 130 (withdrawn): The composition of claim 64 or 74, wherein the valency platform molecule comprises 2,2'-ethylenedioxydiethylamine.

Claim 131 (withdrawn): The composition of claim 64 or 74, wherein the valency platform molecule comprises -CH₂(CH₂OCH₂)_rCH₂-.

Claim 132 (withdrawn): The composition of claim 80, wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.

Claim 133 (withdrawn): The composition of claim 84 wherein the conjugate comprises linking groups that bind the valency platform molecule to the biologically active molecules.

Claim 134 (new): The conjugate of claim 106 or 107, wherein each of the polynucleotides comprises about 20 nucleotides.

Claim 135 (new): A method of making the composition of claim 22, 64 or 106, wherein the biologically active molecules comprise a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is about 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 136 (new): A method of making the conjugate of claims 26, 68 or 107, the method comprising:

reacting (a) a multiplicity of single-stranded polynucleotides, each of which is about 20 nucleotides in length and has a functional group at or proximate one of its termini which is

derivatized with a linker group, with (b) attachment sites on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotide conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.

Claim 137 (new): The composition of claim 26, 68 or 106, wherein the polynucleotide is a single stranded polynucleotide.

Claim 138 (new): The composition of claim 69, wherein the branching groups are derived from a functional moiety selected from the group consisting of diamino acid, triamine, and amino diacid.

Claim 139 (new): The composition of claim 69, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 140 (new): A method of making the composition of claim 89, wherein the method comprises bonding the linker molecules to the polynucleotides and bonding the linker-polynucleotide to the valency platform molecule at the attachment sites to form the conjugate.

Claim 141 (new): A method of making the composition of claim 89, wherein the method comprises bonding the linker molecules to the valency platform molecule at the attachment sites and bonding the linker-valency platform molecule to the polynucleotides to form the conjugate.

Claim 142 (new): A method of making the composition of claim 129, the method comprising forming said conjugates by covalently bonding the polynucleotides to the chemically-defined valency platform molecule via a linker.

Claim 143 (new): The composition of claim 64, wherein the biologically active molecules are selected from the group consisting of carbohydrates, lipids, lipopolysaccharides, peptides, proteins, glycoproteins, and drugs.

Claim 144 (new): The composition of claim 77, wherein the composition is suitable for the suppression of antibody production.

Claim 145 (new): The composition of claim 77, wherein the composition is suitable for the treatment of human systemic lupus erythematosus.

Claim 146 (new): The composition of claim 77, wherein the composition is suitable for reducing antibody levels.

Claim 147 (new): The composition of claim 77 wherein at least one molecule of the biologically active molecules is an analog of an immunogen that binds specifically to an antibody to which the immunogen binds specifically and lacks T cell epitopes.

Claim 148 (new): The composition of claim 66, wherein the biologically active molecules comprise a polynucleotide.

Claim 149 (new): A method of making the composition of claim 114, wherein the method comprises bonding the linker molecule to the biologically active molecule and bonding the linker-biologically active molecule to the valency platform molecule at the attachment sites to form the conjugate.

Claim 150 (new): A method of making the composition of claim 114, wherein the method comprises bonding the linker molecule to the valency platform molecule at the attachment sites and bonding the linker-valency platform molecule to the biologically active molecules to form the conjugate.

Claim 151 (new): The composition of claim 26, 68 or 106, wherein the polynucleotides comprise polynucleotide duplexes having significant binding activity for human systemic lupus erythematosus anti-dsDNA autoantibodies.

Claim 152 (new): The composition of claim 151, wherein the polynucleotides comprise at least 20 base pairs.

Claim 153 (new): The composition of claim 151, wherein the polynucleotides comprise about 20 base pairs.

Claim 154 (new): The composition of claim 151, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 155 (new): The composition of claim 26, 38, 68, 69, 70, 107 or 127, wherein the composition comprises a pharmaceutically acceptable carrier.

Claim 156 (new): A method of making the composition of claim 64 or 106, wherein the biologically active molecules are a polynucleotide duplex, the method comprising forming said conjugates by:

reacting a multiplicity of single-stranded polynucleotides, each of which is at least 20 nucleotides in length and has a functional group at or proximate one of its termini, with functional groups on the chemically-defined valency platform molecule to form the conjugate; and

annealing complementary single-stranded polynucleotides to the single-stranded polynucleotides conjugated to the chemically-defined valency platform molecule to form pendant chains of double-stranded polynucleotides.